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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,009	05/03/2005	Ruth Chiquet-Ehrismann	1-32411A/FMI	1199
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NOVARTIS CORPORATE INTELLECTUAL PROPERTY ONE HEALTH PLAZA 104/3 EAST HANOVER, NJ 07936-1080			EXAMINER GUSSOW, ANNE	
			ART UNIT 1643	PAPER NUMBER
			MAIL DATE 10/10/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/509,009

Applicant(s)

CHIQUET-EHRISMANN ET AL.

Examiner

Anne M. Gussow

Art Unit

1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 August 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-72 is/are pending in the application.
- 4a) Of the above claim(s) 1-10 and 14-52 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 58, 59 and 65-67 is/are allowed.
- 6) ☒ Claim(s) 11-13, 53-57, 60-64 and 68-72 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

DETAILED ACTION

1. Claims 53-72 have been added.
2. Claims 11-13 and 53-72 are under examination.
3. The following Office Action contains NEW GROUNDS of Rejection.

Objections Withdrawn

4. The objections to the specification are withdrawn in view of applicant's amendments to the specification.
5. The objections to claims 11 and 13 are withdrawn in view of applicant's amendment to the claims.

Rejections Withdrawn

6. The rejection of claims 12 and 13 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendment to the claims.
7. The rejection of claims 11-13 under 35 U.S.C. 101 as being directed to non-statutory subject matter is withdrawn in view of applicant's amendments to the claims.

Rejections Maintained/NEW GROUNDS of Rejection

Claim Objections

8. Claim 11 is objected to because of the following informalities: in line 2 the edited claim reads "amino acid sequence shown SEQ ID No. 4", the claim should read "amino acid sequence shown in SEQ ID No. 4".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 53-57, 60-64, and 68-72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated antibody that specifically recognizes amino acid residues 791-1054 of tenascin W for the manufacture of a medicament for treatment of breast cancer, does not reasonably provide enablement for an isolated antibody that specifically recognizes tenascin W for the prophylaxis of just any cancer or the treatment of just any cancer or a disease or condition characterized by excessive bone growth. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 1 12, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are broadly drawn to an isolated antibody that specifically recognizes tenascin W, for the manufacture of a medicament, wherein said tenascin W has a stem cell differentiation activity, wherein said medicament is for the prophylaxis or treatment of cancer, wherein said cancer is metastatic, wherein said cancer is a solid tumor, wherein said cancer is a glioblastoma, prostate, lung, colorectal, osteo- or breast carcinoma, wherein said medicament is for the prophylaxis or treatment of any disease or condition characterized by excessive bone growth.

The specification discloses an antibody that specifically recognizes the tenascin W amino acids 791-1054 of SEQ ID No. 4 (see examples 4 and 5). The specification discloses treatment of metastatic breast cancer in a transgenic mouse model system by administering the tenascin W antibody (see example 6). The specification does not disclose treatment of glioblastoma, prostate, lung, colorectal, or osteo- carcinoma. The specification does not disclose prophylaxis of cancer. The specification does not disclose treatment of disease characterized by excessive bone growth.

When given the broadest reasonable interpretation the prophylaxis of cancer encompasses the prophylaxis of any type of cancer in an individual who has yet to develop said cancer. Thus, it would be necessary to know what type of cancer would develop in a specific organ or tissue and to be able to predict what cell type and/or antigen would be the target. The specification does not provide any teachings of the broadly claimed prophylaxis of cancer, how to determine the individuals who will develop a particular cancer, nor how to effectively prevent said particular cancer type before occurrence, nor does the specification teach the how to predict when a cancer would occur in any individual or the optimal time before such a occurrence to administer the antibody of the instant invention. Thus, one of skill in the art would not be able to use the composition of the invention as a prophylactic treatment without undertaking to determine how to select for individuals which will develop a particular cancer type before the said cancer occurs in the individual.

Regarding the development of a prophylactic immune response it is noted that the abstract of Wheeler (Salud p'ublica de M'exico, 1997. Vol. 39 pages 283-7) teaches that a cancer vaccine against human papillomavirus for the treatment of cervical cancer requires not only the activation of antigens and overcoming the host response, but the generation of high levels of T and B memory cells; and the persistence of antigens. The instant specification has not provided any teachings regarding the persistence of the tumor antigens in an individual who has yet to develop a specific type of cancer. Further, Efferson et al (Anticancer Research, 2005. Vol. 25, pages 715-24) teach that efficient induction of memory cells is hindered by the lack of information about the

relationship between TCR stimulation and the cytokines required for Ag-specific memory CD8⁺ cells and proliferation and survival. It is noted that the instant specification has not provided any evidence that adequate levels of T and B memory cells would persist in an immunized individual who has not developed a cancer, therefore the enablement for how to generate adequate memory T and B cells can not be provided from the general knowledge of in the art. Bachman et al (Journal of Immunology, 2005. Vol. 175, pages 4677-4685) teach that memory T cells are not a homogeneous population and can be divided into central memory T cells with a substantial capacity for recall proliferation and effector memory T cells with limited recall proliferation capacity. Bachman et al teach that the protective capacity of the different subpopulations of memory T cells vary and the generation of the subpopulations is influenced by the nature and route of immune challenge. These references serve to demonstrate that the prior art is not mature with respect to how to elicit an effective prophylactic memory cell response that will persist in an individual not harboring a tumor cells and which would function to protect said individual from tumor cell development.

There is insufficient evidence or nexus that would lead the skilled artisan to predict the ability to induce tumor immunity to prevent tumor production and to eliminate existing tumors by treating an individual with an antibody that recognizes tenascin W. The specification does not teach how inoculating an individual with an antibody that recognizes tenascin W overcomes the back-and-forth struggle between host and tumor, a process which creates highly resistant, poorly immunogenic, and extremely aggressive clones of tumor cells. The specification does not teach how to treat a

disease or condition characterized by excessive bone growth.

In view of the lack of predictability of the art to which the invention pertains and the lack of established clinical protocols for effective cancer therapies, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to prophylactically treat cancer and absent working examples providing evidence which is reasonably predictive that the claimed treatments are effective for vaccinating individuals against cancer, commensurate in scope with the claimed invention.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. The rejection of claims 11-13 and newly added claims 53-57 under 35 U.S.C. 102(e) as being anticipated by Ni, et al. is maintained.

The response filed August 20, 2007 has been carefully considered but is deemed not to be persuasive. The response states that the homology between the human tenascin W of the invention (as seen in, e.g., SEQ ID No. 4 of the present application)

and the Ni reference SEQ ID No. 29 is about 6.5% overall. [The homology encompasses a total of 84 residues, which represent about 6.5% of the entirety of the human tenascin W of the invention, i.e., 1294 residues.] It is extremely unlikely, if not impossible, that a peptide fragment constituting about 6.5% identity to a full length protein possesses the same biological activities as said full length protein (see response page 11).

In response to this argument, while the overall homology between the protein of SEQ ID No. 4 in the instant application and SEQ ID No. 29 of Ni, et al. is 6.5%; the local homology over the C-terminal region of the protein is 84%. The limitations in the claims require an antibody that recognizes the tenascin W protein of SEQ ID No. 4. The limitations do not specifically define the epitope of the protein which must bind the antibody, thus an antibody to the protein of Ni would also recognize the C-terminal portion of the instant protein of SEQ ID No. 4 (tenascin W). Additionally, the limitations contained in the wherein clauses of the claims do not add patentable weight to the claims, which are drawn to an antibody, since the limitations are an intended use of the antibody.

Therefore, after a fresh consideration of the claims and the evidence provided, all the limitations of the claims have been met.

Conclusion

13. Claims 58, 59, and 65-67 are in condition for allowance.

Claims 11-13, 53-57, 60-64, and 68-72 are rejected.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571) 272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

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Status information for unpublished applications is available through Private PAIR only.

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Anne M. Gussow

October 3, 2007

~~LARRY R. HELMS, PH.D.~~
~~SUPERVISORY PATENT EXAMINER~~


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